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PREDICTING RISK OF PELVIC FLOOR DISORDERS 12 AND 20 YEARS AFTER DELIVERY

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Declaration of interests

Jelovsek – Royalties, UpToDate; Chagin – No conflicts; Barber – Royalties, UpToDate, Elsevier; Maria Gyhagen – Honoraria - Astellas Pharma for speaker participation; Suzanne Hagen – No conflicts; Don Wilson – No conflicts; Michael Kattan – No conflicts; Andrew Elders – University of Gothenburg; Bjorn Areskoug – No conflicts; Christine MacArthur – No conflicts; Ian Milsom – Grant (National LUA/ALF Grant no 11315), Honorarium for lecture (SCA, Astellas, Allergan).

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ABSTRACT

Background: Little progress has been made in preventing pelvic floor disorders despite their significant health and economic impact. Identifying women at risk remains a key element in targeting prevention and planning health resource allocation strategies. Although events around the time of childbirth are clinically recognized as important predictors, it is difficult to counsel women and intervene around the time of childbirth due to an inability to accurately convey a patient's risk in the presence of multiple risk factors and the long time lapse, often decades, between obstetric events and the onset of pelvic floor disorders later in life. Prediction models and scoring systems have been used in other areas of medicine to identify patients at risk for chronic diseases. Models have been developed for use before delivery that predict short-term risk of pelvic floor disorders after childbirth but no models predicting long-term risk exist.

Objective: To use variables known before and during childbirth to develop and validate prognostic models estimating risks of these disorders 12 and 20 years after delivery.

Study Design: Obstetric variables were collected from two cohorts: 1) women who gave birth in the United Kingdom and New Zealand (n=3763) and 2) women from the Swedish Medical Birth Register (n=4991). Pelvic floor disorders were self-reported 12 years after childbirth in the UK/NZ cohort and 20 years after childbirth in the Swedish Register. The cohorts were split so that data during the first half of the cohort's time period were used to fit prediction models and validation was performed from the second half (temporal validation). As there is currently no consensus on how to best define pelvic floor disorders from a patient's perspective, we chose to fit the data for each model using multiple outcome definitions for prolapse, urinary incontinence, fecal incontinence, 1 or more pelvic floor disorder and 2 or more pelvic floor disorders. Model accuracy was measured: 1) by ranking an individual's risk among all subjects in the cohort (discrimination) using a concordance index and 2) by observing whether the predicted probability was too high or low (calibration) at a range of predicted probabilities using visual plots.

Results: Models were able to discriminate between women who developed bothersome symptoms or received treatment, at 12 and 20 years respectively, for: pelvic organ prolapse (concordance indices 0.570, 0.627), urinary incontinence (concordance indices 0.653, 0.689), fecal incontinence (concordance indices 0.618, 0.676), ≥ 1 pelvic floor disorders (concordance indices 0.639, 0.675) and ≥ 2 pelvic floor disorders (concordance indices 0.635, 0.619). The discriminatory ability of all models is shown in Table 2. Route of delivery and family history of each pelvic floor disorder were strong predictors in most models. Urinary incontinence before and during the index pregnancy was a strong predictor for developing all pelvic floor disorders in most models 12 years after delivery. The 12 and 20-year bothersome or treatment for prolapse models were accurate when providing predictions for risk from 0% to approximately 15%. The 12-year and 20-year primiparous model began to over-predict when risk rates reached 20%. When predicting bothersome symptoms or treatment for urinary incontinence, the 12-year models were accurate when predictions ranged from approximately 5% to 60% and 20-year primiparous models were accurate between 5% and 80%. For bothersome symptoms or treatment for fecal incontinence, the 12 and 20-year models were accurate between 1% and 15% risk and began to over-predict at rates above 15% and 20%, respectively.

Conclusion: Models may provide an opportunity before birth to identify women at low risk of developing pelvic floor disorders and institute prevention strategies such as pelvic floor muscle training, weight control or elective cesarean section for women at higher risk. Models are provided at:

http://riskcalc.org/UR_CHOICE/

INTRODUCTION

Pelvic floor disorders such as pelvic organ prolapse, urinary incontinence and fecal incontinence constitute a huge global health problem affecting millions of women throughout the world. The prevalence of pelvic floor disorders has been reported to be 46% and many women have more than one.¹ Pelvic floor disorders can have a negative influence on a woman's well-being, quality of life, body image and sexual function, and prevent many from participating in recreational and sporting activities.^{1,2} The global costs of pelvic floor disorders to health care systems and society are enormous.^{1,3} Approximately, 1 in 5 women will undergo surgery for prolapse or urinary incontinence by age 85.^{4,5} Current treatments, often surgical, carry risks and relatively high rates of recurrence.^{6,7}

Little progress has been made in preventing pelvic floor disorders despite their significant health and economic impact.⁸ Identifying women at risk remains a key element in targeting prevention and planning health resource allocation strategies. The etiology of pelvic floor disorders is known to be multifactorial and obstetric trauma during childbirth is one of the most important identifiable risk factors.¹ Numerous epidemiological studies indicate an increased prevalence of pelvic floor disorders with increasing parity with the greatest increase in risk attributed to the birth of the first child.¹ Although events around the time of childbirth are clinically recognized as important predictors, many women undergo the labor and delivery process and do not experience long-term pelvic floor dysfunction. At present, it is difficult to counsel women and intervene around the time of childbirth due to an inability to accurately convey a patient's risk in the presence of multiple risk factors and the long time lapse, often decades, between obstetric events and the onset of pelvic floor disorders later in life.

Prediction models and scoring systems have been used in other areas of medicine to identify patients at risk for chronic diseases.^{9,10} Models have been developed for use before delivery that predict short-term risk of pelvic floor disorders after childbirth but no models predicting long-term risk exist.^{11,12} The aims of this study were to construct and validate models capable of predicting the development of pelvic floor disorders 12 and 20 years after delivery using data from two large independent international cohort studies.^{13,14} Such models have potential to provide individual women more accurate predictions than the

current standard of care given: 1) the paucity of existing tools, 2) the large amount of variability in the predicted rates of pelvic floor disorders provided by clinicians in practice and 3) the increasing evidence that clinical prediction models consistently show superiority over expert clinicians because they avoid common cognitive biases.^{15, 16}

METHODS

This study is reported using methods set forth in the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD): the TRIPOD Statement.¹⁷ The study population consisted of two longitudinal, prospective cohort studies. The PROlapse and incontinence LONG-term (ProLong) study aimed to determine whether delivery mode was predictive of pelvic floor disorders in 10,989 primiparous and multiparous women 12 years after the index birth.¹⁴ The second cohort was the Swedish Pregnancy, Obesity and Pelvic Floor (SwePOP) study. The aim of SwePOP was to compare the prevalence of pelvic floor disorders in a cohort of 10,117 primiparous women identified from the Swedish Medical Birth Register 20 years after one delivery.^{13, 18} Both studies were designed to investigate delivery mode as a predictor of pelvic floor disorders and therefore, captured key maternal, labor and delivery variables that were known at that time to be potential risk factors of pelvic floor disorders. Study details have been previously published and are summarized in [Figure 1](#).^{14, 18}

In the ProLong study, prolapse symptoms were measured using the validated Pelvic Organ Prolapse Symptom Score.¹⁹ Urinary and fecal incontinence questions were designed by the study team because at the time of recruitment (1993/94) there were no suitable validated questionnaires on incontinence. Family history was measured using a response of either “yes” or “no” to, “Have any of your blood relatives ever had a prolapse?” and “If yes, how are they related to you (eg. mother, sister)?” In the SwePOP study, prolapse was defined using the validated sPOP questionnaire,²⁰ urinary incontinence using the Sandvik severity scale,²¹ and fecal incontinence using the Wexner score.²² Family history was measured using a response of either yes or no to each of the following items, “Has your mother suffered from urinary

leakage?”, “Has your mother suffered from prolapse?” and “Has your mother suffered from leakage of flatus/gas or feces?” Each study received ethics committee approval at all centers. Written informed consent was obtained from participants in both studies.

In order to allow for temporal validation, each cohort was temporally split so that women giving birth in the first half of the cohort’s time period were considered for the training dataset and used to build each model. For the ProLong dataset, data from primiparous and multiparous women who gave birth between September 11, 1993 and May 1, 1994 and responded at 12 years (N=2,095) were used to build models to predict 12-year outcomes for women who gave birth between May 2, 1994 and November 11, 1994 (N=1,668). Similarly, in the SwePOP dataset, data from primiparous women who gave birth between January 1, 1985 and June 30, 1987 (N=2,607) were used to build models to predict 20-year outcomes for women who gave birth between July 1, 1987 and December 31, 1988 (N=2,384). For each training dataset, the multiple imputation using chained equations (MICE) method was used to calculate missing values for predictors.²³ Predictors for the test dataset and outcomes for all models were based on actual, not imputed values.

As there is currently no consensus on how to best define pelvic floor disorders from a patient’s perspective, we chose to fit the data for each model using multiple outcome definitions for prolapse, urinary incontinence, fecal incontinence, 1 or more pelvic floor disorder and 2 or more pelvic floor disorders. We developed models to predict: 1) the presence of “any symptoms” regardless of severity; 2) the presence of bothersome symptoms; 3) treatment for the disorder, or 4) the combination of either bothersome symptoms or receiving treatment for each disorder (prolapse, urinary incontinence, fecal incontinence) and their combination (any pelvic floor disorder or 2 or more pelvic floor disorders) (Table 1 footnote). Data are only presented for category 4) above, and all remaining outcomes are available in the supplementary results.

Multiple logistic regression models were fit to the training data consisting of the full set of candidate predictors and each outcome. Harrell's "Model Approximation" process of backwards elimination was used to rank the variables in order of importance starting from the full model using a bootstrap bias-corrected concordance index as the stopping criteria to find the best parsimonious model.²⁴ Variables with individual p-values that were greater than 0.05 were left in the model if they offered information to improve the overall model accuracy. Removal was evaluated by determining which variable had the smallest effect on the R^2 and was stopped when the bootstrap concordance index had a change less than 0.01. This process provided a parsimonious model for each outcome.

Model accuracy was measured: 1) by ranking an individual's risk among all subjects in the cohort (discrimination) using a concordance index and 2) by observing whether the predicted probability was too high or low (calibration) at a range of predicted probabilities using visual plots. Once the models were built and prior to performing temporal validation, all concordance indices were internally validated using 1,000 bootstrap samples to adjust for overfitting biases on the initial build and 95% confidence intervals were calculated. Calibration curves along with distributions of predicted probabilities of those with and without each outcome were generated to visually observe how close model predictions were to actual predictions.

Temporal validation requires a prognostic model to produce accurate predictions when it is tested in cohorts from different time periods. It is a prospective form of validation recommended when an independent validation data set with similar obstetric populations and long-term outcomes is not available.¹⁷ Models were developed using antepartum variables, previous delivery variables and delivery mode. We specifically investigated whether events that occurred at the time of delivery (e.g. episiotomy, perineal laceration) significantly improved the accuracy of prediction by comparing the difference in accuracy using a bootstrap method from their respective receiver operating characteristic curve.

All models were combined into a single integrated web-based calculator so that a complete set of predictors can be entered and outcomes for all pelvic floor disorders are presented. All analyses were performed using R Version 3.2.3 (2015-12-10).

RESULTS

Baseline characteristics and outcomes were available in 3763 participants in the ProLong study 12 years after their index birth and 4991 of the participants in the SwePOP study 20 years after their first and only birth. The overall rates of pelvic floor disorders with 95% confidence intervals 12 and 20 years after delivery are described in Table 1. The descriptive statistics of candidate predictors among each study cohort are provided in [Supplemental Table 1](#).

Model Discrimination

Forty separate models were developed from the two cohorts for use including 20 models that predict outcomes in primiparous and multiparous women 12 years after delivery and 20 models that predict outcomes in primiparous women 20 years after delivery. All 40 final models included predictors known or estimated prior to delivery along with actual route of delivery. Each model's discriminatory ability is shown in [Table 2](#). Models were able to discriminate between women who developed bothersome symptoms or received treatment, at 12 and 20 years respectively, for pelvic organ prolapse (concordance indices 0.570, 0.627), urinary incontinence (concordance indices 0.653, 0.689), fecal incontinence (concordance indices 0.618, 0.676), one or more pelvic floor disorders (concordance indices 0.639, 0.675) and two or more pelvic floor disorders (concordance indices 0.635, 0.619).

Model Calibration

Calibration curves for the models from the two cohorts predicting bothersome pelvic floor disorders or the need for treatment at 12 and 20 years are shown in [Figure 2](#). The majority of models predicted probabilities close to actual probabilities throughout a range of clinically useful predictions but began to

over-predict at higher probabilities. The 12 and 20-year bothersome or treatment for prolapse models were accurate when providing predictions for risk from 0% to approximately 15% (Table 1 average risk 7-10%). The 12-year and 20-year primiparous model began to over-predict when risk rates reached 20%. When predicting bothersome symptoms or treatment for urinary incontinence, the 12-year models were accurate when predictions ranged from approximately 5% to 60% (Table 1 average risk 23-31%) and 20-year primiparous models were accurate between 5% and 80% (Table 1 average risk 18-20%). For bothersome symptoms or treatment for fecal incontinence, the 12 and 20-year models were accurate between 1% and 15% risk (Table 1 average risk 3-7%). The bothersome or treatment for fecal incontinence models began to over-predict at rates above 15% and 20% for the 12 and 20-year model, respectively. A complete set of calibration curves for models predicting all outcomes at 12 and 20 years are available in Supplemental Figures [1A](#) and [1B](#). An online calculator (http://riskcalc.org/UR_CHOICE/) is available for clinical use and two examples of predictions for a hypothetical average and high-risk patient are displayed. (Supplemental Figure [2A](#) and [2B](#))

Model Variables

The relative influence of each predictor for models predicting the combination of bothersome symptoms or receiving treatment for each disorder is summarized in [Figure 3](#). Route of index delivery, number of previous births and family history of each pelvic floor disorder were the most influential in most models. Any urinary incontinence before pregnancy was an influential predictor for women developing bothersome prolapse or having treatment for prolapse, urinary incontinence and fecal incontinence 12 years after delivery. In primiparous women at 20 years, having a vaginal delivery was significantly associated with increasing a woman's 20-year risk of developing bothersome or treatment for prolapse and urinary incontinence. The strength of association among the predictors for all models are provided in Supplemental Figures [3A](#) and [3B](#).

DISCUSSION

Most women undergo childbirth without experiencing bothersome pelvic floor disorders or requiring treatment for pelvic floor disorders throughout their lifespan. More recently, women are seeking more evidence-based informed decision making prior to labor that will reassure them that the birthing process will not be detrimental to their long-term health. Informing a woman of her risks of pelvic floor disorders along with other risks of childbirth, is in accordance with the judgment of the 2015 United Kingdom Supreme Court case and supports a woman's autonomy and her right to informed choice regarding her care in pregnancy and childbirth.²⁵ A major barrier to effective prevention of pelvic floor disorders is the inability to identify "at risk" women to target prevention programs. Childbirth is among the most important and consistent risk factor for pelvic floor disorders, however, in most women, clinically relevant symptoms and treatment occur decades later in life.²⁶ The models presented, while not perfect, predict better than chance and are able to discriminate between those with and without pelvic floor disorders 51-75% of the time. Traditionally, when estimates of risk are provided to women during pregnancy, they are based on a clinician's knowledge and experience, by quoting overall average population risk to all women, or by heuristically assigning individuals into crude categories such as low or high-risk groups. Even when high-level evidence exists, estimates are typically provided without accurately accounting for the specifics of a woman's unique characteristics such as her age, parity, co-morbidities and family history. The development and implementation of accurate clinical tools that go beyond clinical judgment and predict an individual woman's future risk of developing pelvic floor disorders will be an essential component of any primary prevention strategy and will help reassure the majority of mothers when serious pelvic floor damage is not strongly predicted.

We developed models for multiple definitions of each pelvic floor disorder outcome, combined into a single, easy-to-use, on-line calculator. The models allow calculation of risk that includes past delivery characteristics and planned route of delivery (vaginal versus cesarean section). The role of elective cesarean section in the prevention of pelvic floor disorders remains controversial and, given the potential maternal and fetal risks, is unlikely to be an effective prevention strategy for most women.^{26, 27} It has been

estimated, for instance, that approximately 9 cesarean sections would be necessary to prevent urinary incontinence in one primiparous woman of average risk.¹⁸ However, a strategy of offering cesarean section to women who are at substantially higher than average risk for pelvic floor disorders may be a more appropriate and effective prevention strategy. At what risk threshold that occurs is currently unknown however, and must be balanced against the risks of cesarean section and, in many cases, multiple repeat cesarean deliveries, especially since maximum protection may occur when all deliveries are by Cesarean.^{14,26} After delivery, the models are intended for women who may be considering other secondary prevention strategies. Prevention strategies such as pelvic floor muscle training and weight loss programs offer promise but have not been adequately studied long-term or many years after delivery.²⁸ Compliance with long-term prevention programs is a significant challenge and may be improved by informing women about their individual risk of developing the disorders.²⁹

The major strengths of this analysis are the application of predictive analytics to two large well-described cohorts of women that collected common maternal and obstetrical variables and similarly defined pelvic floor disorder outcomes 12 and 20 years after delivery. While not racially diverse, together these cohorts do provide important geographic and cultural diversity, which are important for conditions affecting quality of life. However, there are important differences in the two cohorts. The ProLong dataset includes primiparous and multiparous women and reports outcomes at 12 years after delivery, while the SwePOP study included only primiparous women and reported outcomes at 20 years after delivery. Because of these differences, we chose not to develop our prediction models in one cohort and then externally validate them in the other as is commonly done. Instead, we performed temporal validation in each separate cohort, which is a stronger approach than the more commonly performed random splitting of a dataset into a development and validation cohort.¹⁷

An important limitation of our models is that they are not perfect. In spite of this, they advance our current abilities to predict an individual's risk of developing pelvic floor disorders many years after

childbirth better than providing highly variable, average event rates. The models in this analysis provide similar discrimination to other predictive models currently used in clinical practice whose concordance indices generally range from 0.6 to 0.8 including widely-used models such as the National Cancer Institute Gail model for prediction of Breast Cancer risk (concordance index 0.59) and the Framingham Cardiovascular Risk Model (concordance index 0.72).^{9,30} While the models developed in this analysis were well calibrated at clinical decision-making thresholds, some models provide higher than actual probabilities when rates of actual outcomes are high and where there were fewer outcome events available.

In summary, the models provide individualized prediction of risk of developing pelvic floor disorders 12 and 20 years after delivery using maternal and obstetrical variables available prior to childbirth. These models should help identify high-risk women in whom prevention strategies such as pelvic floor muscle training and weight control or elective cesarean section might be targeted. Ideally, external validation of the models should be conducted when and if other large cohorts with similar follow-up become available.

REFERENCES

1. MILSOM I, ALTMAN D, CARTWRIGHT R, ET AL. Epidemiology of Urinary Incontinence (UI) and other Lower Urinary Tract Symptoms (LUTS), Pelvic Organ Prolapse (POP) and Anal Incontinence (AI). In: Abrams P, Cardozo L, Khoury S, Wein A, eds. *5th International Consultation on Incontinence*. Paris: Health Publications, Ltd., 2013.
2. COYNE KS, SEXTON CC, IRWIN DE, KOPP ZS, KELLEHER CJ, MILSOM I. The impact of overactive bladder, incontinence and other lower urinary tract symptoms on quality of life, work productivity, sexuality and emotional well-being in men and women: results from the EPIC study. *BJU Int* 2008;101:1388-95.
3. MOORE K, WAGNER TH, SUBAK L, et al. Economics of urinary and faecal incontinence, and prolapse. In: Abrams P, Cordozo L, Koury S, Wein A, eds. *Incontinence*. Paris: Health Publications Ltd., 2012.
4. HAYA N, BAESSLER K, CHRISTMANN-SCHMID C, et al. Prolapse and continence surgery in countries of the Organization for Economic Cooperation and Development in 2012. *Am J Obstet Gynecol* 2015;212:755 e1-55 e27.
5. WU JM, MATTHEWS CA, CONOVER MM, PATE V, JONSSON FUNK M. Lifetime risk of stress urinary incontinence or pelvic organ prolapse surgery. *Obstet Gynecol* 2014;123:1201-6.
6. FORD AA, ROGERSON L, CODY JD, OGAH J. Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev* 2015:CD006375.
7. MAHER C, FEINER B, BAESSLER K, SCHMID C. Surgical management of pelvic organ prolapse in women. *The Cochrane database of systematic reviews* 2013;4:CD004014.
8. NIDDK, OFFICE OF RESEARCH ON WOMEN'S H, NATIONAL INSTITUTE ON A. Prevention of Lower Urinary Tract Symptoms in Women: Bladder Health Clinical Centers (PLUS-CCs) (U01). National Institutes of Health, 2014 website: <https://grants.nih.gov/grants/guide/rfa-files/RFA-DK-14-004.html>.
9. D'AGOSTINO RB, SR., GRUNDY S, SULLIVAN LM, WILSON P, GROUP CHDRP. Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. *JAMA* 2001;286:180-7.
10. LYSENKO V, JONSSON A, ALMGREN P, et al. Clinical risk factors, DNA variants, and the development of type 2 diabetes. *N Engl J Med* 2008;359:2220-32.
11. JELOVSEK JE, PICCORELLI A, BARBER MD, TUNITSKY-BITTON E, KATTAN MW. Prediction models for postpartum urinary and fecal incontinence in primiparous women. *Female Pelvic Med Reconstr Surg* 2013;19:110-8.
12. WILSON D, DORNAN J, MILSOM I, FREEMAN R. UR-CHOICE: can we provide mothers-to-be with information about the risk of future pelvic floor dysfunction? *Int Urogynecol J* 2014;25:1449-52.
13. GYHAGEN M, BULLARBO M, NIELSEN TF, MILSOM I. Prevalence and risk factors for pelvic organ prolapse 20 years after childbirth: a national cohort study in singleton primiparae after vaginal or caesarean delivery. *BJOG* 2013;120:152-60.
14. MACARTHUR C, GLAZENER C, LANCASHIRE R, HERBISON P, WILSON D, PROLONG STUDY G. Exclusive caesarean section delivery and subsequent urinary and faecal incontinence: a 12-year longitudinal study. *BJOG* 2011;118:1001-7.
15. JELOVSEK JE, CHAGIN K, BRUBAKER L, et al. A model for predicting the risk of de novo stress urinary incontinence in women undergoing pelvic organ prolapse surgery. *Obstet Gynecol* 2014;123:279-87.
16. KATTAN MW, O'ROURKE C, YU C, CHAGIN K. The Wisdom of Crowds of Doctors: Their Average Predictions Outperform Their Individual Ones. *Med Decis Making* 2016;36:536-40.

17. COLLINS GS, REITSMA JB, ALTMAN DG, MOONS KG. Transparent reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD): the TRIPOD statement. *J Clin Epidemiol* 2015;68:134-43.
18. GYHAGEN M, BULLARBO M, NIELSEN TF, MILSOM I. The prevalence of urinary incontinence 20 years after childbirth: a national cohort study in singleton primiparae after vaginal or caesarean delivery. *BJOG* 2013;120:144-51.
19. HAGEN S, GLAZENER C, SINCLAIR L, STARK D, BUGGE C. Psychometric properties of the pelvic organ prolapse symptom score. *BJOG* 2009;116:25-31.
20. TEGERSTEDT G, MIEDEL A, MAEHLE-SCHMIDT M, NYREN O, HAMMARSTROM M. A short-form questionnaire identified genital organ prolapse. *J Clin Epidemiol* 2005;58:41-6.
21. SANDVIK H, HUNSKAAR S, SEIM A, HERMSTAD R, VANVIK A, BRATT H. Validation of a severity index in female urinary incontinence and its implementation in an epidemiological survey. *J Epidemiol Community Health* 1993;47:497-9.
22. JORGE JM, WEXNER SD. Etiology and management of fecal incontinence. *Dis Colon Rectum* 1993;36:77-97.
23. WHITE IR, ROYSTON P, WOOD AM. Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med* 2011;30:377-99.
24. HARRELL FE. *Regression modeling strategies: with applications to linear models, logistic regression, and survival analysis*. New York: Springer.
25. SOKOL DK. Update on the UK law on consent. *BMJ* 2015;350:h1481.
26. LANDEFELD CS, BOWERS BJ, FELD AD, et al. National Institutes of Health state-of-the-science conference statement: prevention of fecal and urinary incontinence in adults. *Ann Intern Med* 2008;148:449-58.
27. VISCO AG, VISWANATHAN M, LOHR KN, et al. Cesarean delivery on maternal request: maternal and neonatal outcomes. *Obstet Gynecol* 2006;108:1517-29.
28. HAGEN S, GLAZENER C, MCCLURG D, et al. Pelvic floor muscle training for secondary prevention of pelvic organ prolapse (PREVPROL): a multicentre randomised controlled trial. *Lancet* 2017;389:393-402.
29. NATIONAL CANCER I. *Theory at a Glance: A guide for health promotion practice*. National Institutes of Health: US Department of Health and Human Services, National Institutes of Health, 2012 (vol 2016).
30. ROCKHILL B, SPIEGELMAN D, BYRNE C, HUNTER DJ, COLDITZ GA. Validation of the Gail et al. model of breast cancer risk prediction and implications for chemoprevention. *J Natl Cancer Inst* 2001;93:358-66.

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Jelovsek – Royalties, UpToDate; Chagin – No conflicts; Barber – Royalties, UpToDate, Elsevier; Maria Gyhagen – Honoraria - Astellas Pharma for speaker participation; Suzanne Hagen – No conflicts; Don Wilson – No conflicts; Michael Kattan – No conflicts; Andrew Elders – University of Gothenburg; Bjorn Areskoug – No conflicts; Christine MacArthur – No conflicts; Ian Milsom – Grant (National LUA/ALF Grant no 11315), Honorarium for lecture (SCA, Astellas, Allergan).

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Analysis and interpretation of data - Jelovsek, Chagin, Gyhagen, Hagen, Wilson, Kattan, Elders, Barber, Areskoug, MacArthur, Milsom

Drafting of the manuscript - Jelovsek, Chagin, Gyhagen, Hagen, Wilson, Kattan, Elders, Barber, Areskoug, MacArthur, Milsom

Critical revision of the manuscript for important intellectual content - Jelovsek, Chagin, Gyhagen, Hagen, Wilson, Kattan, Elders, Barber, Areskoug, MacArthur, Milsom

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2. Figure 2 – Calibration curves for before delivery models predicting bothersome pelvic floor disorder or needing treatment for a pelvic floor disorder 12 and 20 years after delivery. The horizontal axis is the predicted probability provided by the model and the vertical axis is the actual probability of the outcome. Plots were inspected for predicted probabilities to remain close to actual probabilities (the 45-degree line) within the range of probabilities where patient or clinical decisions are made. When the dotted line is under the dashed 45-degree line the model provides predictions that are higher than actual probabilities (over-prediction) and if the dotted line is over the dashed 45-degree line the model provides predictions that are lower than actual probabilities (under-prediction).
3. Figure 3 – Odds ratios for predictors in the models predicting bothersome pelvic organ prolapse, urinary incontinence or fecal incontinence or needing treatment for these conditions 12 and 20 years after delivery. POP, pelvic organ prolapse; UI, urinary incontinence; FI, fecal incontinence.

Each box indicates the odd ratio of each variable included in the model with horizontal line indicating the 95% CI. If the horizontal line and box are green then the variable was significant at a level of 0.05. An arrow indicates that the line or the odd ratio extend off of the plot.

4. Supplementary Figure 1 – Calibration curves for all models predicting pelvic floor disorders 12 (Figure 1A) and 20 years (Figure 1B) after delivery.
5. Supplementary Figure 2 – Example of the UR-CHOICE online calculator for models predicting pelvic floor disorders 20 years after delivery. Figure 2A and 2B show a 28-year-old primigravid woman who weighs 150 pounds, height is 5 feet 4 inches, estimated infant weight is 7 pounds 2 ounces, head circumference is 35 cm, and has no history of urinary incontinence before or during pregnancy. The average risk patient (Figure 2A) has no family history of pelvic organ prolapse, urinary or fecal incontinence and the high-risk patient (Figure 2B) has a positive family history of pelvic organ prolapse and urinary incontinence as well as urinary incontinence during her pregnancy.
6. Supplementary Figure 3 – Odds ratio of each variable included in before delivery models predicting pelvic floor disorders 12 (Figure 3A) and 20 (Figure 3B) years after delivery. Each box indicates the odd ratio of each variable included in the model with horizontal line indicating the 95% CI. If the horizontal line and box are green then the variable was significant at a level of 0.05. An arrow indicates that the line or the odd ratio extend off of the plot.

Table 1 Overall rates of pelvic floor disorders with 95% confidence intervals in primiparous and multiparous women 12 years after childbirth in the ProLong study and in primiparous women 20 years after childbirth in the SwePop study

			Any		Bothersome		Treatment		Bothersome or Treatment
	Parity	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)
Pelvic organ prolapse⁺									
12-years	0	291	17% (15.1%, 18.7%)	102	6% (4.8%, 7.0%)	28	2% (1.2%, 2.6%)	126	8% (7.0%, 9.8%)
20-years	0	646	13% (12.1%, 14.0%)	300	6% (5.4%, 6.7%)	73	1.5% (1.2%, 1.9%)	346	7% (6.6%, 8.1%)
12-years	≥1	347	17% (15.4%, 18.7%)	111	5% (4.5%, 6.4%)	61	3% (2.6%, 4.3%)	159	9% (7.6%, 10.3%)
Urinary incontinence⁺⁺									
12-years	0	877	51% (48.5%, 53.3%)	380	22% (20.2%, 24.2%)	83	5% (3.9%, 6.0%)	423	25% (23.2%, 27.4%)
20-years	0	1895	38% (36.9%, 39.6%)	822	17% (15.7%, 17.8%)	163	3% (2.9%, 3.9%)	902	19% (17.9%, 20.1%)
12-years	≥1	1103	54% (52.0%, 56.4%)	510	25% (23.5%, 27.3%)	113	6% (4.7%, 6.8%)	564	29% (26.8%, 30.8%)
Fecal incontinence⁺⁺⁺									
12-years	0	203	12% (10.3%, 13.4%)	42	2% (1.7%, 3.2%)	37	2% (1.5%, 2.9%)	68	4% (3.2%, 5.1%)
20-years	0	671	14% (12.6%, 14.5%)	112	2% (1.8%, 2.7%)	54	1% (0.8%, 1.4%)	145	3% (2.5%, 3.5%)
12-years	≥1	283	14% (12.5%, 15.5%)	74	4% (2.8%, 4.5%)	56	3% (2.1%, 3.6%)	109	6% (4.5%, 6.6%)
≥1 Pelvic floor disorders									
12-years	0	1031	60% (57.7%, 62.3%)	461	27% (25.0%, 29.2%)	132	9% (7.6%, 10.6%)	528	35% (32.4%, 37.2%)
20-years	0	2322	47% (45.7%, 48.5%)	1051	22% (20.3%, 22.7%)	265	6% (5.1%, 6.5%)	1163	25% (24.0%, 26.5%)
12-years	≥1	1255	62% (59.7%, 63.9%)	590	29% (27.4%, 31.4%)	197	12% (10.1%, 13.1%)	680	38% (35.8%, 40.3%)
≥2 Pelvic floor disorders									
12-years	0	298	17% (15.5%, 19.1%)	60	3.5% (2.6%, 4.4%)	15	1% (0.4%, 1.4%)	74	4% (3.5%, 5.4%)
20-years	0	743	15% (14.0%, 16.0%)	167	3% (2.9%, 3.9%)	25	0.5% (0.3%, 0.7%)	185	4% (3.3%, 7.1%)
12-years	≥1	406	20% (18.3%, 21.7%)	97	5% (3.9%, 5.7%)	31	1.5% (1.0%, 2.1%)	120	6% (5.1%, 7.2%)

+ Pelvic organ prolapse was defined at 12 years using responses to, “Do you have a feeling of something coming down from or in your vagina?” Any pelvic organ prolapse was defined as responses: occasionally, sometimes, most of the time, or all of the time. Bothersome pelvic organ prolapse was defined as responses: sometimes, most of the time, or all of the time. At 20 years, pelvic organ prolapse was defined using responses to, “Do you have a feeling of something bulging from your vagina?” Any pelvic organ prolapse was defined as responses: infrequently, sometimes, or often. Bothersome pelvic organ prolapse was defined as responses of sometimes or often.

++ Urinary incontinence was defined at 12 years using responses to, “Do you ever lose urine when you don’t mean to?” and if yes, “in the last month how often has this happened, on average?” Any urinary incontinence was defined using responses: < 2x per month, weekly, or 3 or more times a day and bothersome urinary incontinence was defined as responses: weekly or 3 or more times a day. At 20 years, urinary incontinence was defined using responses to, “Do you have involuntary leakage of urine?” and if yes, “how often has this happened, on average?” Any incontinence was defined as responses: < 2x per month, weekly, 3 or more times a day and bothersome urinary incontinence was defined as responses: weekly or 3 or more times a day.

+++ Fecal incontinence was defined at 12 years using responses to the question, “Do you ever lose control of bowel motions (stool/faeces) from your back passage in between visits to the toilet?” Any fecal incontinence was defined as responses: occasionally, sometimes, most of the time, or all of the time. Bothersome FI was defined as responses most of the time and all of the time. At 20 years, having fecal incontinence was defined as responses to the Wexner scale questions, “Do you have involuntary leakage of solid faeces?” or “Do you have involuntary leakage of liquid faeces?” Any fecal incontinence was defined as responses to either question as: less than once a month (rarely), once a month but less than once a week (sometimes), greater than once a week but less than once a day (usually) or once or more every day (always). Bothersome fecal incontinence was defined using the question, “Has involuntary leakage of liquid or solid faeces influenced your feeling of frustration?” Responses of moderately or very much were considered bothersome while responses of not at all or a little were not bothersome.

Table 2 The discriminatory ability of models predicting risk of pelvic floor disorders 12 and 20 years after birth

Outcome	Year	Model Build		Temporal Validation	
		Concordance index	95% CI	Concordance index	
Pelvic organ Prolapse					
Any	12	0.623	(0.591, 0.653)	0.598	
	20	0.680	(0.648, 0.712)	0.619	
Bothersome	12	0.660	(0.612, 0.706)	0.598	
	20	0.736	(0.695, 0.779)	0.606	
Treatment	12	0.734	(0.667, 0.804)	0.560	
	20	0.809	(0.739, 0.870)	0.751	
Bothersome or Treatment	12	0.644	(0.603, 0.683)	0.570	
	20	0.751	(0.714, 0.791)	0.627	
Urinary Incontinence					
Any	12	0.672	(0.650, 0.696)	0.641	
	20	0.714	(0.692, 0.734)	0.695	
Bothersome	12	0.702	(0.677, 0.730)	0.640	
	20	0.691	(0.665, 0.717)	0.684	
Treatment	12	0.651	(0.602, 0.702)	0.712	
	20	0.685	(0.625, 0.745)	0.634	
Bothersome or Treatment	12	0.704	(0.679, 0.731)	0.653	
	20	0.698	(0.673, 0.724)	0.689	
Fecal Incontinence					
Any	12	0.605	(0.570, 0.636)	0.586	
	20	0.648	(0.619, 0.677)	0.624	
Bothersome	12	0.640	(0.569, 0.710)	0.638	
	20	0.720	(0.658, 0.788)	0.658	
Treatment	12	0.687	(0.620, 0.750)	0.542	
	20	0.674	(0.571, 0.759)	0.642	
Bothersome or Treatment	12	0.670	(0.616, 0.721)	0.618	
	20	0.701	(0.644, 0.759)	0.676	
≥ 1 Pelvic Floor Disorder					
Any	12	0.664	(0.643, 0.688)	0.650	
	20	0.700	(0.681, 0.719)	0.685	
Bothersome	12	0.686	(0.663, 0.713)	0.643	
	20	0.693	(0.668, 0.717)	0.667	
Treatment	12	0.670	(0.628, 0.710)	0.649	
	20	0.656	(0.614, 0.698)	0.623	
Bothersome or Treatment	12	0.687	(0.661, 0.711)	0.639	
	20	0.698	(0.674, 0.722)	0.675	
≥2 Pelvic Floor Disorders					
Any	12	0.648	(0.618, 0.677)	0.581	
	20	0.702	(0.673, 0.729)	0.676	
Bothersome	12	0.730	(0.680, 0.781)	0.661	

Outcome	Year	Model Build		Temporal Validation
		Concordance index	95% CI	Concordance index
Treatment	20	0.760	(0.707, 0.808)	0.621
	12	0.738	(0.650, 0.831)	0.711
Bothersome or Treatment	20	0.600	(0.507, 0.744)	0.513
	12	0.706	(0.644, 0.751)	0.635
	20	0.753	(0.705, 0.802)	0.619

Year 12 includes data from the ProLong dataset and year 20 includes data from SwePop dataset

Supplemental Table 1 Candidate predictors of pelvic floor disorders in the Swedish pregnancy, obesity and pelvic floor study and the prolapse and incontinence long-term study

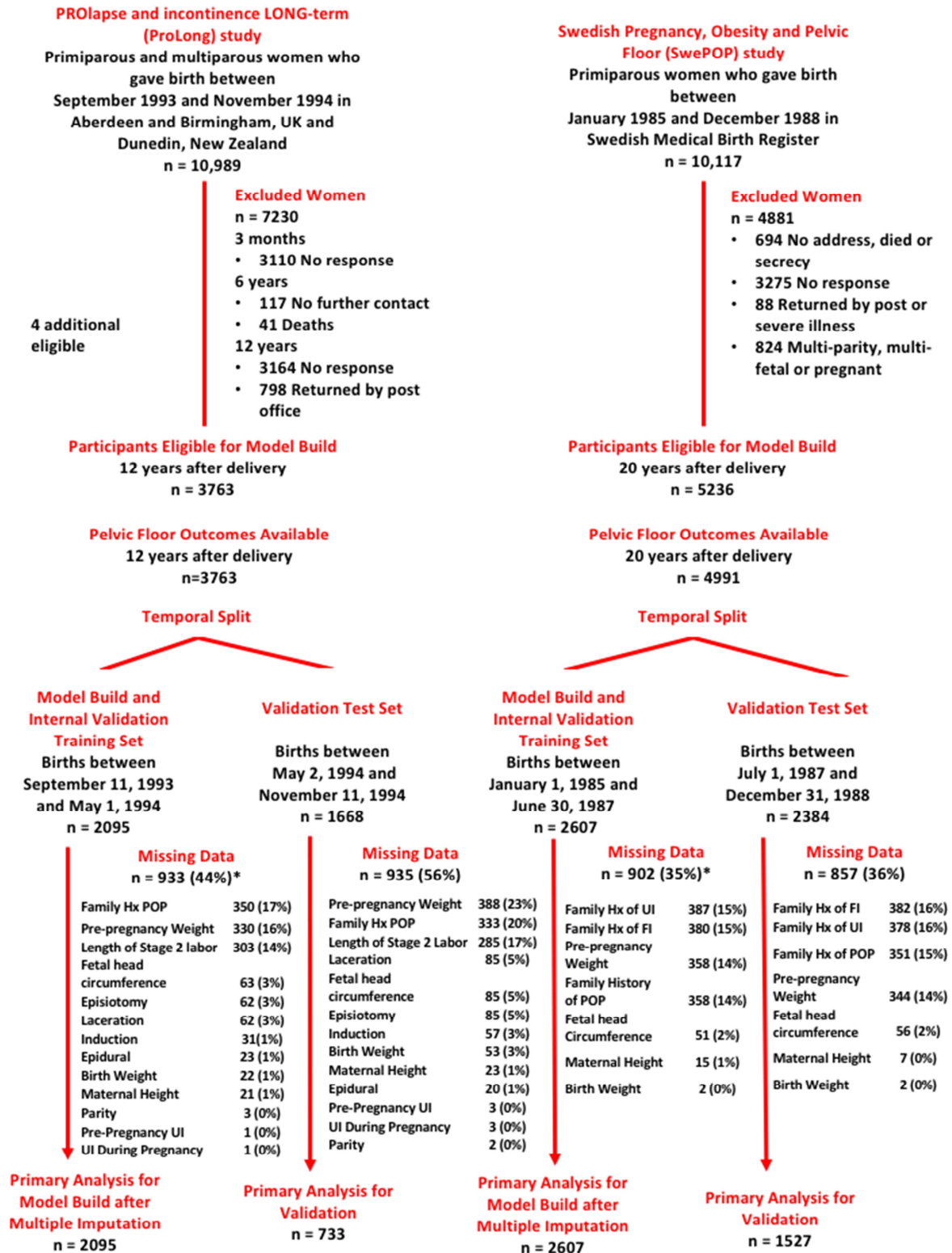
Variables		ProLong N = 3,763	SwePop N = 4,991
Maternal Age at Delivery		29 (26, 32)	29 (25, 34)
	Missing	0 (0%)	0 (0%)
Maternal Pre-Pregnancy Weight (kg)		60 (54, 67)	62 (56, 70)
	Missing	718 (19%)	702 (14%)
Maternal Height (cm)		163 (159, 168)	167 (163, 170)
	Missing	44 (1%)	22 (0%)
Number of Previous Births		1 (0, 1)	NA
	Missing	5 (0%)	
	0	1723 (46%)	
	1	1389 (37%)	
	2	453 (12%)	
	3	144 (4%)	
	≥ 4	49 (1%)	
Route of Delivery (Index Birth)			
	Vaginal Unassisted	2556 (68%)	3061 (61%)
	Vacuum	193 (5%)	726 (15%)
	Forceps	401 (11%)	22 (0%)
	C-Section Elective	271 (7%)	764 (15%)
	C-Section Acute	342 (9%)	418 (8%)
Number of Past Unassisted Vaginal Deliveries		1 (0, 2)	NA
	Missing	10 (1%)	
	0	1067 (28%)	
	1	1404 (37%)	
	2	891 (24%)	
	3	269 (7%)	
	≥4	122 (3%)	
Number of Past Forceps Assisted Deliveries		0 (0, 0)	NA
	Missing	10 (1%)	
	0	2868 (76%)	
	1	835 (22%)	
	2	44 (1%)	
	3	6 (0%)	
Number of Past Vacuum Assisted Deliveries		0 (0, 0)	NA
	Missing	10 (1%)	
	0	3515 (93%)	
	1	236 (6%)	
	2	2 (0%)	
Number of Past Planned C-Sections		0 (0, 0)	NA
	Missing	10 (0%)	
	0	3370 (90%)	
	1	316 (8%)	
	2	58 (2%)	
	≥ 3	9 (0%)	
Number of Past Acute C-Sections		0 (0, 0)	NA
	Missing	10 (0%)	
	0	3277 (87%)	

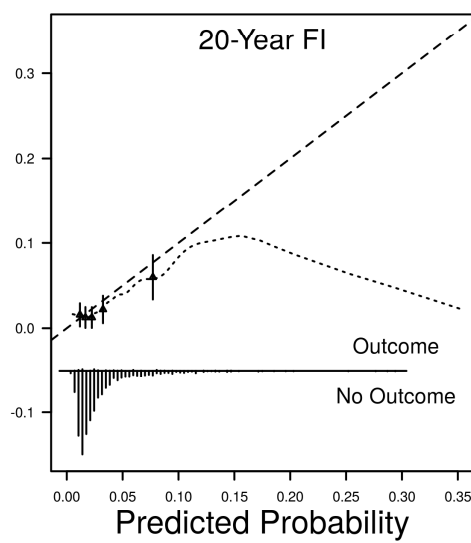
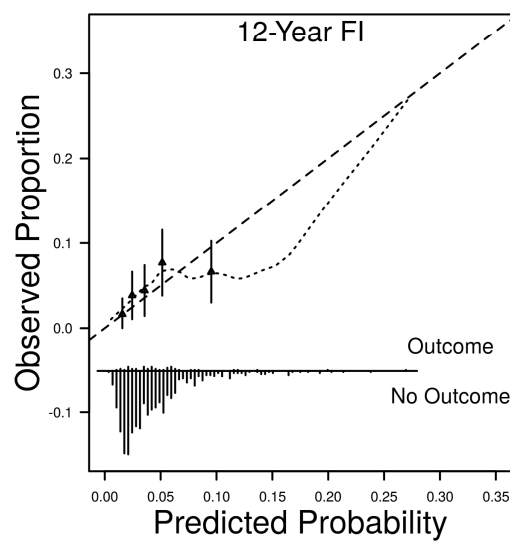
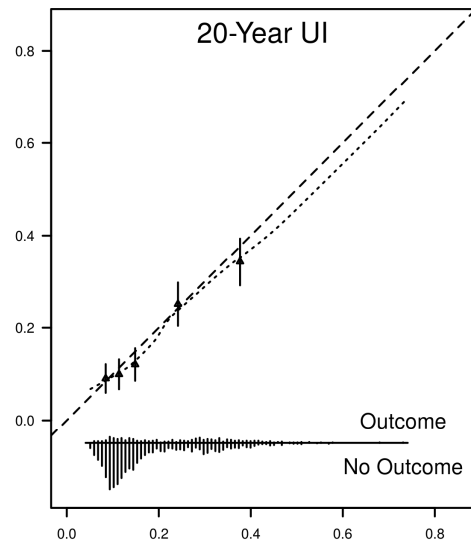
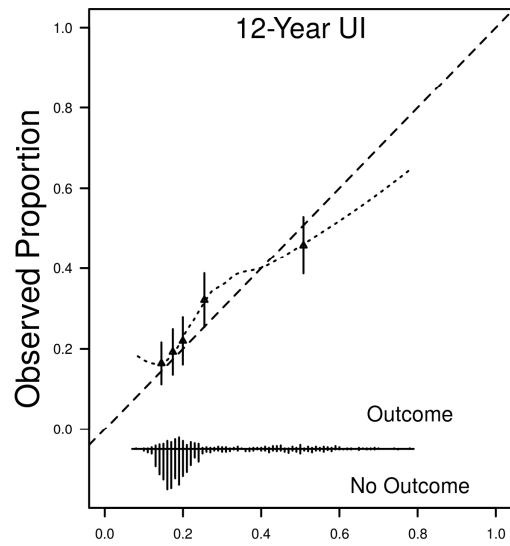
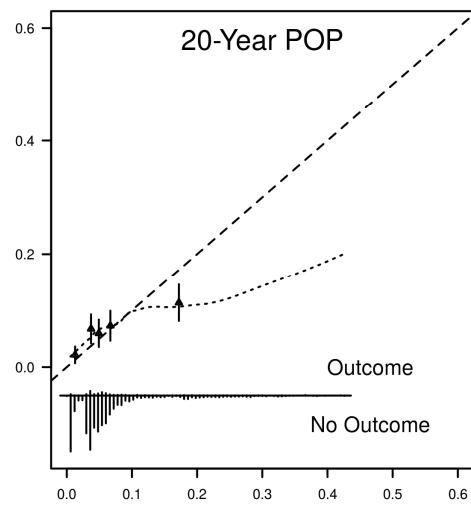
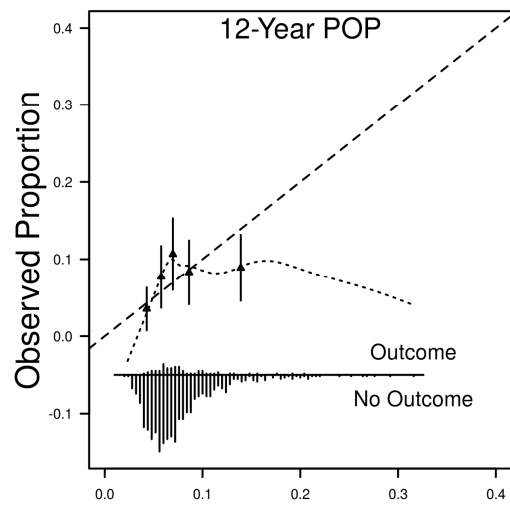
Variables		ProLong N = 3,763	SwePop N = 4,991
	1	436 (12%)	
	2 & 3	40 (1%)	
Number of Any Past Vaginal Deliveries	1 (1, 2)		NA
	Missing	10 (1%)	
	0	478 (13%)	
	1	1583 (42%)	
	2	1169 (31%)	
	3	365 (10%)	
	≥ 4	158 (4%)	
Number of Any Past C-Sections	0 (0, 0)		NA
	Missing	10 (1%)	
	0	2999 (80%)	
	1	570 (15%)	
	2	149 (4%)	
	≥ 3	35 (1%)	
Family History of POP	Yes	615 (16%)	676 (14%)
	No	2465 (66%)	3606 (72%)
	Missing	683 (18%)	709 (14%)
Family History of UI	NA		
	Yes		1374 (28%)
	No		2852 (57%)
	Missing		765 (15%)
Family History of FI	NA		
	Yes		629 (13%)
	No		3600 (72%)
	Missing		762 (15%)
Pre-Pregnancy UI			NA
	Yes	382 (10%)	
	No	3377 (90%)	
	Missing	4 (0%)	
UI During Pregnancy			NA
	Yes	386 (10%)	
	No	3373 (90%)	
	Missing	4 (0%)	
Infant Birthweight (g)		3435 (3080, 3760)	3520 (3160, 3960)
	Missing	75 (2%)	4 (0%)
Infant Head Circumference (cm)		34.7 (34, 35.7)	35 (34, 36)
	Missing	148 (4%)	107 (2%)
Twins			NA
	Yes	81 (2%)	
	No	3682 (98%)	
	Missing	0 (0%)	
Induction Performed			NA
	Yes	646 (17%)	
	No	3029 (80%)	
	Missing	88 (2%)	
Epidural Used During Labor			

Variables		ProLong N = 3,763	SwePop N = 4,991
Episiotomy Performed	Yes	1196 (32%)	1499 (30%)
	No	2524 (67%)	3492 (70%)
	Missing	43 (1%)	0 (0%)
2nd, 3rd, or 4th Degree Perineal Laceration Occurred	Yes	819 (22%)	510 (10%)
	No	2797 (74%)	4481 (90%)
	Missing	147 (4%)	0 (0%)
Time in Second Stage (min.)	Yes	1430 (38%)	174 (3%)
	No	2186 (58%)	4817 (97%)
	Missing	147 (4%)	0 (0%)
		28 (8, 85)	NA
	Missing	588 (16%)	

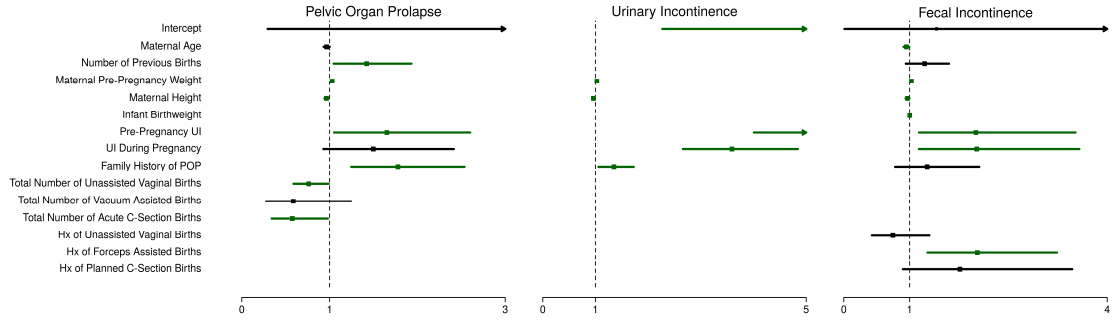
SwePoP, Swedish Pregnancy, Obesity and Pelvic Floor (SwePOP) study; ProLong, PROlapse and incontinence LONG-term (ProLong) study; NA, Not available.

Data are n (%) or median (interquartile range) unless otherwise specified. Variables are relative to the index delivery.

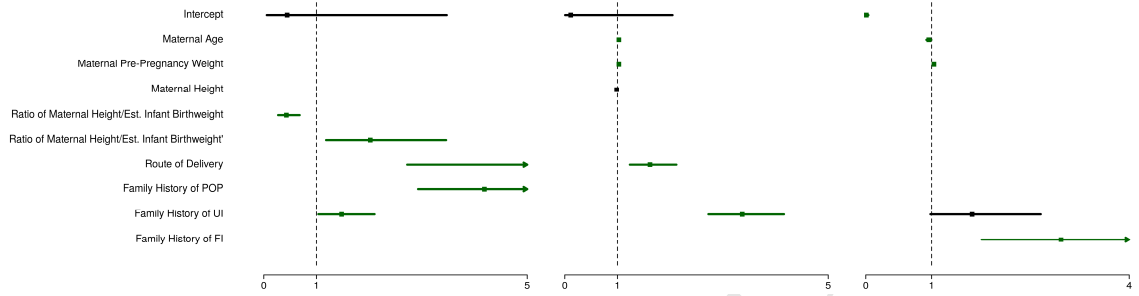


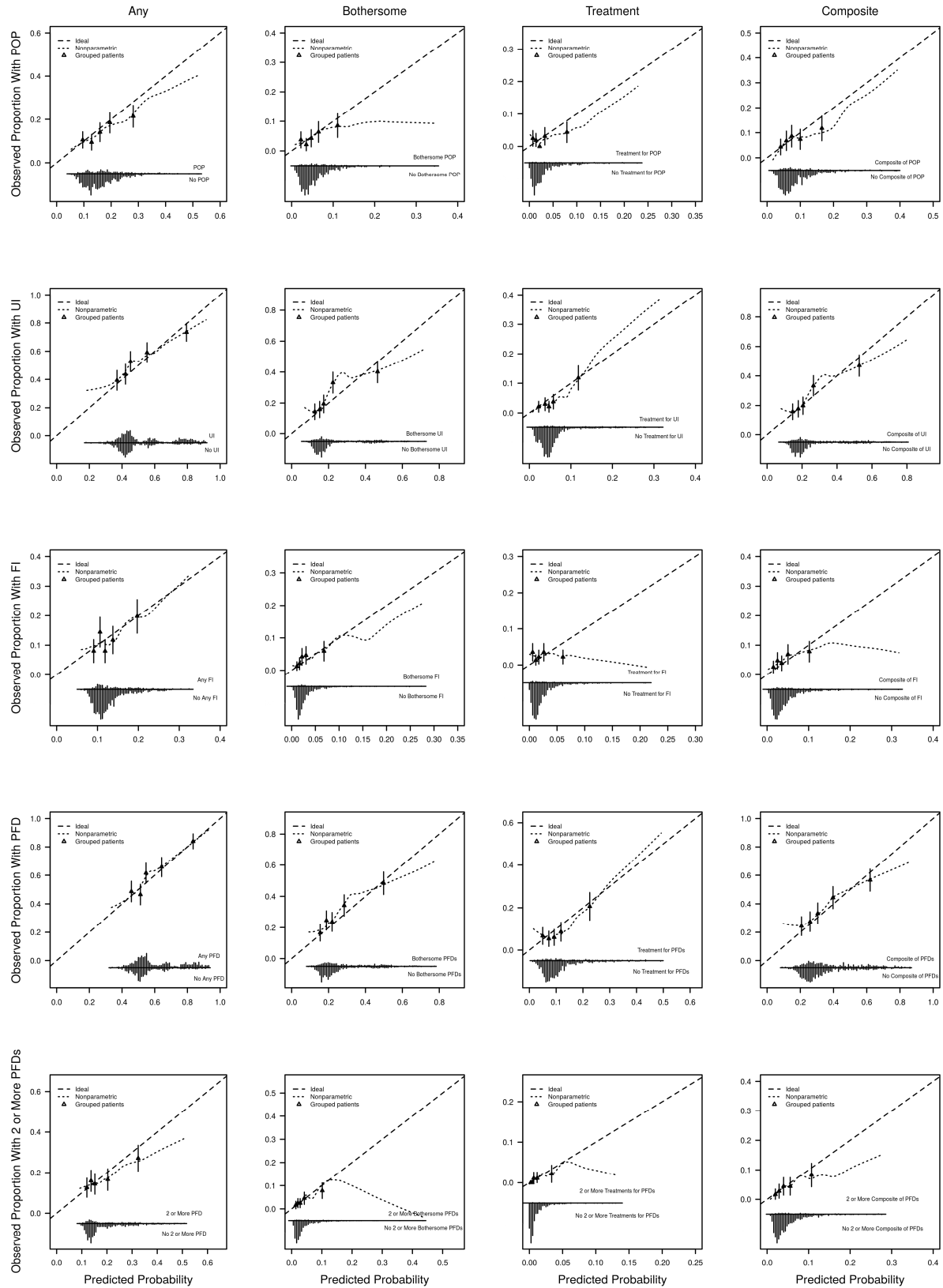


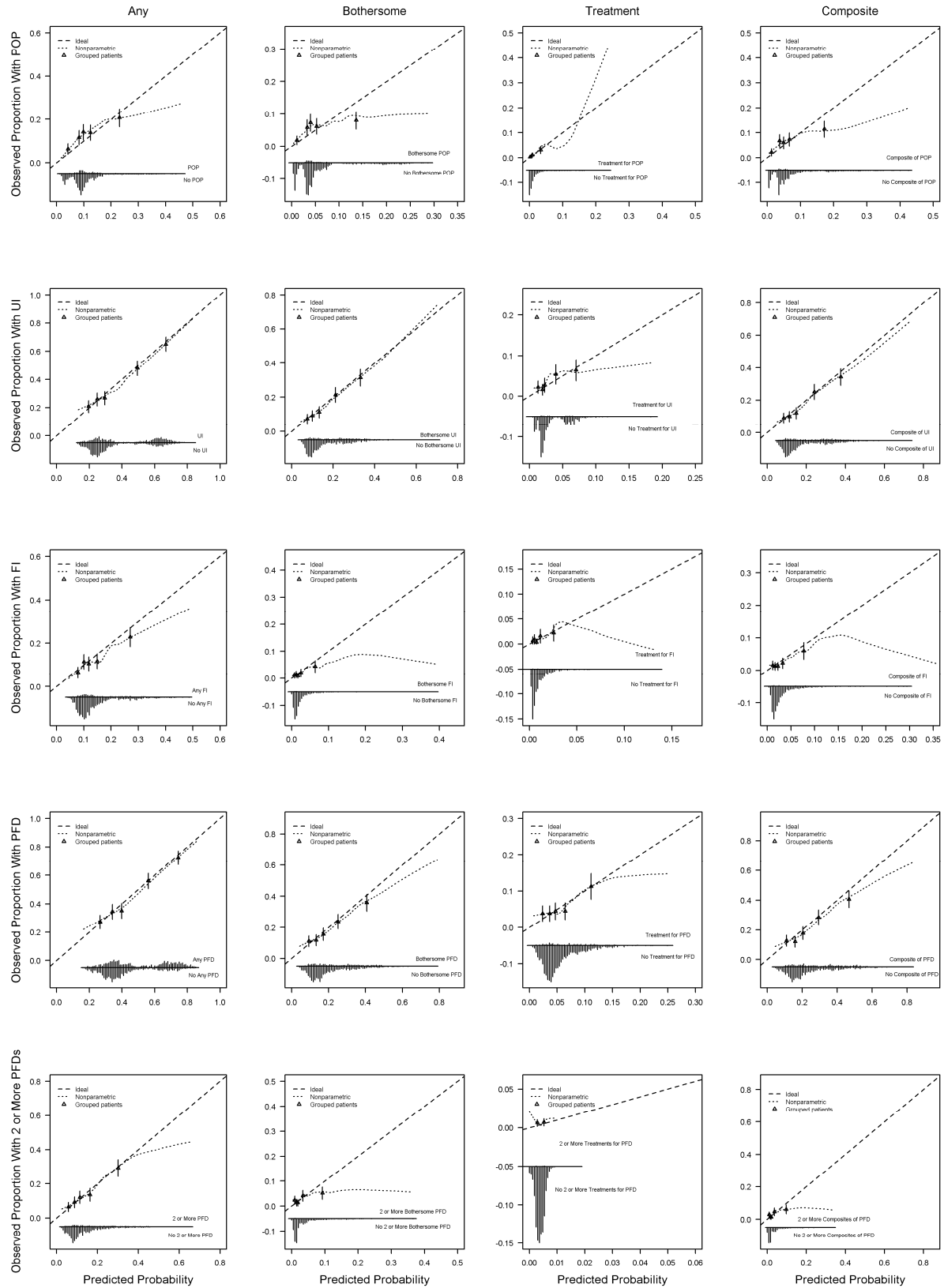
12-Year Bothersome or Treatment for
Models Before Delivery



20-Year Bothersome or Treatment for
Models Before Delivery







Outcomes	Route of Delivery	Any	Bothersome	Treatment	Bothersome or Treatment	Average Risk of Bothersome or Treatment
Pelvic Organ Prolapse	Vaginal	10%	3%	1%	4%	9%
	C-Section	3%	1%	<0.5%	1%	3%
Urinary Incontinence	Vaginal	30%	14%	2%	15%	20%
	C-Section	20%	10%	1%	10%	15%
Fecal Incontinence	Vaginal	14%	3%	1%*	2%	3%
	C-Section	10%	1%	2%*	2%	3%
Any Pelvic Floor Disorder	Vaginal	40%	18%	4%	20%	27%
	C-Section	26%	10%	2%	12%	18%
Two or More Pelvic Floor Disorders	Vaginal	13%	2%	<0.5%	2%	4%
	C-Section	6%	1%	<0.5%	1%	2%

Outcomes	Route of Delivery	Any	Bothersome	Treatment	Bothersome or Treatment	Average Risk of Bothersome or Treatment
Pelvic Organ Prolapse	Vaginal	29%	>10%	3%	20%	9%
	C-Section	12%	5%	<0.5%	5%	3%
Urinary Incontinence	Vaginal	68%	33%	7%	>30%	20%
	C-Section	55%	25%	3%	27%	15%
Fecal Incontinence	Vaginal	14%	3%	1%*	4%	3%
	C-Section	10%	1%	2%*	4%	3%
Any Pelvic Floor Disorder	Vaginal	72%	>40%	10%	48%	27%
	C-Section	57%	28%	6%	33%	18%
Two or More Pelvic Floor Disorders	Vaginal	32%	>10%	<0.5%	>10%	4%
	C-Section	17%	5%	<0.5%	6%	2%

